REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 1, 8, 9 and 12 are amended and claims 10 and 11 are cancelled without prejudice or disclaimer. Support for the amendments may be found throughout the application and claims as originally filed, and so no new matter has been added. Upon entry of the amendments, claims 1-8 and 12 will be pending . Claim 9 is currently withdrawn pursuant to the Restriction Requirement, which Applicants continue to traverse, as set forth below. Thus Applicants urge consideration of claims 1-8, 9 and 12.

I. Withdrawal of the Restriction Requirement / Request For Rejoinder

Applicants acknowledge that the Examiner has made the restriction requirement final, however Applicants again urge that this requirement is not supported by the governing rules of patent practice. Applicants therefore respectfully request that the Examiner reconsider the restriction requirement in view of the following comments.

In proffering the restriction requirement, the Examiner points to Griesbacher *et al.* (British Journal of Pharmacology *137*(5), 692-700 (November 2002)) as "evidence" that another was in possession of the claims. Office Action, page 2. The Examiner also alleges that "the Griesbacher *et al.* is a 102(f) reference." *Id.* However, this is not a proper grounds for rejection, let alone restriction.

MPEP 2137 states that "[w]here it can be shown that an applicant 'derived' an invention from another, a rejection under 35 USC 102(f) is proper." However, it also provides that "[w]here there is a published article identifying the authorship...that discloses subject matter being claimed in an application under on-going examination, ***the designation of authorship or inventorship does not raise a presumption of inventorship with respect to the subject matter disclosed in the article*** or with respect to the subject matter disclosed but not claimed in the

patent so as to justify a rejection under 35 U.S.C. 102(f)." Emphasis added. Thus, the fact that Griesbacher names as authors individuals who are not named as inventors on the captioned application does not in and of itself raise an issue under §102(f). Moreover, because there is no other indication that Applicants derived the invention from the other authors on Griesbacher, a §102(f) rejection would be improper.

The Examiner's original grounds for restriction were based upon the assertion that at least one Markush group "is not novel" in view of Griesbacher. However, as noted previously, Griesbacher is not prior art to the instant application. Thus, the basis of the restriction is improper. While the Office Action now cites Griesbacher as a §102(f) reference, Applicants are not aware of any provision of the PCT Unity of Invention rules that permits restriction on the basis of "derivation." Moreover, as shown above, the record here does not support a §102(f) rejection.

The Restriction Requirement also is improper under the PCT rules because it restricts claims directed to a compound and claims directed to methods of using that compound. The Examiner alleges that "[i]n the instant case the method of treating, for example, inflammation can be practice[d] with aspirin/cox 2 inhibitors." Restriction Requirement, page 4. However, claim 9 is not directed to any method of treating inflammation, but instead recites a method of treating inflammation using the recited compound, which is the same compound recited in claim 1. Thus, claim 1 and claim 9 share a single inventive concept, e.g., the novel and non-obvious compound. Under PCT Rules 13.1, 13.2 and the cited Annexes, claim 9 should be examined with claim 1.

Applicants therefore respectfully submit that the Restriction Requirement is wholly improper and should be withdrawn.

Request for Rejoinder

After withdrawing the restriction requirement, the Examiner is requested to rejoin claim 9 for examination in the present application.

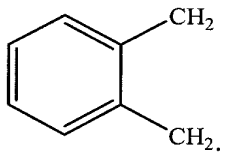
II. Rejections Under 35 U.S.C. § 112, Second Paragraph.

Claim 1

Claim 1 stands rejected under 35 U.S.C. §112, second paragraph, for alleged lack of clarity in the phrase "R1 and R2 together are an *o*-xylylene group optionally substituted on the aromatic ring... ." Applicants respectfully traverse this rejection.

Applicants have amended the phrase to recite: "R^1 and R^2 together form an o-xylylene group wherein the aromatic ring moiety of the *o*-xylylene group is optionally substituted..." This amendment is supported by the application as filed, as explained below.

Page 3 of the specification as filed teaches that R^1 and R^2 together may constitute an ortho-xylylene group, which is exemplified as having the formula *o*-$C_6H_4(CH_2)_2$. Structurally, the ortho designation (*o*-) indicates that the methylene groups are attached to the aromatic ring on adjacent carbon atoms; i.e.:



The skilled artisan readily would understand that the two xylylene methylene groups, "CH_2," represent the points of attachment to the remainder of the molecule, resulting in the formation of another six-membered ring that includes R^1 and R^2. For example, the skilled artisan readily would understand that the "-CH_2" groups do not exist independently, but serve as points of attachment. Thus, the teachings in the specification convey to the skilled artisan that the aromatic group of the ortho-xylylene moiety is bound to the remainder of the molecule via the

methylene groups at the positions denoted by R^1 and R^2. Page 3 of the specification also teaches that "[t]he aromatic ring of this xylylene group may optionally be substituted . . . ." and so those of skill in the art will readily understand that the aromatic ring may be substituted by one or more of the stated groups.

In view of the foregoing amendments and explanations, Applicants submit that the claim is clear and respectfully request that the Examiner remove the noted rejection.

Claim 8

Claim 8 stands rejected under 35 U.S.C §112, second paragraph, for alleged indefiniteness for not stating a dosage limitation. Applicants respectfully traverse this ground of rejection. Nevertheless, in order to expedite allowance, Applicants have amended the claim to recite "a therapeutically effective amount." Therefore the grounds for rejection should be moot.

II. Rejections Under 35 U.S.C. § 112, First Paragraph.

Claims 8 and 12

Claims 8 and 12 stand rejected under 35 U.S.C §112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

Although the rejection is applied to both claims 8 and claim 12, the basis of the rejection appears to relate only to claim 12. Thus, the basis for the rejection of claim 8 is not clear. Nevertheless, Applicants believe that the foregoing amendments obviate any enablement issues surrounding claim 8.

With respect to claim 12, while not agreeing on the merits, Applicants have amended the claim to recite the disease conditions being treated. Applicants submit that the grounds for this rejection are now moot.

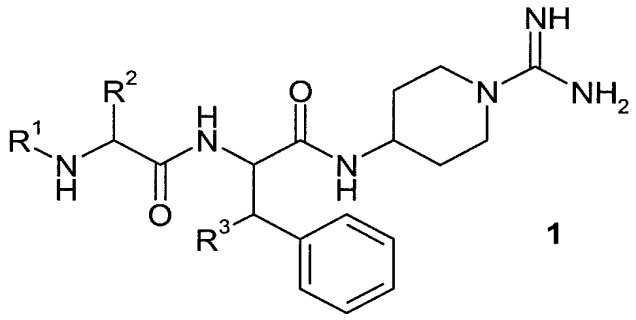
III. Rejection Under 35 U.S.C. § 102(f).

Claims 1-8 and 12 stand rejected under 35 U.S.C §102(f) as anticipated by Griesbacher *et al.* For the reasons discussed above with regard to the requirement for restriction, Applicants respectfully traverse, and request that the Examiner withdraw the rejection. In particular, contrary to the assertion at page 2 of the Office Action, the mere difference between authorship and inventorship does not require Applicants to submit an affidavit. To the contrary, MPEP 2137 expressly states that "the designation of authorship or inventorship does not raise a presumption of inventorship with respect to the subject matter disclosed in the article or with respect to the subject matter disclosed but not claimed in the patent so as to justify a rejection under 35 U.S.C. 102(f)." Moreover, while MPEP 2137 provides that a Rule 132 Declaration may be required "to rebut a rejection under 35 U.S.C. 102(a) or (e)," because Griesbacher is not prior art to the instant application, such a requirement is not proper here. Applicants therefore respectfully request reconsideration and withdrawal of the §102(f) rejection.

IV. Rejection Under 35 U.S.C. § 103.

Claims 1-8 and 12 stand rejected under 35 U.S.C §103(a) as being allegedly unpatentable over WO 93/08211 (McIver) supplemented with CA 119:226431 and CA 139:245221 (instant application) in further view of Garrett *et al.* (*J. Peptide Res.* 52, 62-71 (1998)) and Peake *et al.* (*Clin. Exp. Immunol.* 79, 454-458 (1990)). Applicants point out that the CA for the instant application cannot be used as a basis for rejection. Applicants also believe that the citation to "CA 119:226431" is a typographical error, and that the Chemical Abstract for McIver, CA 119:226432, was intended. Applicants would appreciate clarification of these points in the next Office communication. Applicants respectfully traverse this rejection.

The presently claimed compounds are those of Formula 1:



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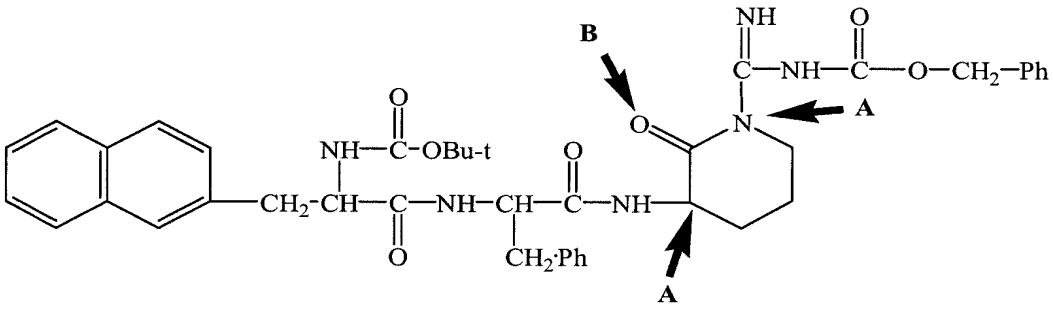
None of the McIver, Garrett, or Peake references teaches or suggests compounds of such a formula, whether viewed alone or in combination. Further, none of these references provides the requisite reasons for one of skill in the art to modify the compounds of those references to arrive at the claimed compounds.

On page 4 of the instant Office Action, the Examiner cites to a compound that is disclosed in McIver and delineated in CA 119:226432. The compound referenced by the Examiner is:



(arrows added by Applicants to highlight different features)

To the skilled artisan, there are several differences between the compounds of McIver and the claimed compounds. First the oxo group at arrow B is absent in the claimed compounds. Second, the compounds of McIver have a piperidinyl group that is connected within the molecule at the 1,3 positions, as shown by arrows A, whereas the claimed compounds have a 1,4 arrangement.

The Office Action alleges that equivalence of the presence and absence of an oxo group on the piperidine was taught by Garrett and Peake. However, Garrett and Peake do not in fact teach such equivalence. Moreover, there is no reason found in any of the cited references to modify the McIver compounds to arrive at the presently claimed compounds.

Applicants first direct the Examiner's attention to the fact that the cited structure of McIver is an intermediate in a chemical synthetic pathway. Thus, it is not the type of compound that one of skill in the art would have a reason for modifying. The compound cited by the Examiner is used in a synthetic pathway such as that exemplified in Scheme A, on page 15 of McIver. The Examiner will note that in Scheme A, the 1,3 piperidines of McIver are reacted with lithium aluminum hydride (LAH) and hydrogen (H_2) to prepare the Arg-aldehyde groups in the peptide chains. Specifically,compound 3, having a 2-oxo-1,3-piperidinyl group, reacts with LAH and H_2. The result is essentially a reduction of the oxo group to an aldehyde, and a ring opening of the piperidinyl group to form the –Arg- group of compound 4. This final reaction product does not have a piperidinyl group. Thus, the 1,3 piperidines in the intermediary compounds of McIver are merely pecursors for the resulting –Arg- groups. *See* McIver, page 14, lines 19-29.

The 1,3-orientation of the piperidine is essential for McIver's reaction. If the McIver compounds were modified to have a 1,4 orientation, as would be required to lead to the claimed compounds, the McIver compounds would be rendered unsatisfactory for their intended purpose. When such a modification of the prior art is required to arrive at the claimed invention, a §103 rejection is improper. MPEP 2143.01(V) ["The Proposed Modification Cannot Render The Prior Art Unsatisfactory For Its Intended Purpose"].

Those of skill in the art will readily recognize, as will the Examiner, that when the oxo group of McIver's compound is reduced to an aldehyde and the rest of the piperidine is ring-opened, the piperidine ring no longer exists. Thus, there is no suggestion of the claimed compounds. The Examiner's citation to Garrett and Peake does not cure these deficiencies.

Garrett is directed to peptide aldehyde inhibitors of kallikreins. In Garrett, as with McIver, the only disclosure of a compound with an oxo group on a piperidinyl group is in the context of an intermediate, in the reaction schemes at pages 61 and 62. Again, the piperidinyl group is used as a protecting group for the resulting –Arg- residue. And, again, the piperidinyl group is in a 1,3 orientation, in contrast to the 1,4 arrangement in the claimed compunds. Contrary to the assertion in the Office Action, there is no suggestion by Garrett that a piperidinyl group with an oxo is equivalent to a piperidinyl group without an oxo. To the contrary, Garrett requires the oxo group for the reduction/ring opening reaction, to form the Arg-aldehyde.

Peake is directed to peptide inhibitors of complement enzymes. At best, Peake discloses a compound with a piperidinyl group that does not have an oxo group. Like McIver and Garrett, however, the cited compound of Peake does not have a 1,4 arrangement on the piperidine ring. Moreover, the combination of Garrett and Peake in no way suggests that piperidinyl groups with and without an oxo group are equivalent. As discussed above, the cited compound of Garrett is an intermediate, and the piperidinyl group with an oxo is reduced and the piperidinyl group ring opens to leave the Arg-aldehyde in the compounds of Garrett. That reaction would not be possible if the piperidinyl group of Garrett's compounds did not have an oxo. Thus, piperidinyl groups with and without an oxo group are not equivalent in the context of Garrett. Moreover, the Office Action fails to cite any reason that the skilled artisan would turn to the teachings of Peake to modify a compound according to McIver.

The foregoing demonstrates that the cited references fail in all respects to teach or suggest the claimed compounds. There are no teachings that would lead the skilled artisan to modify the compounds of McIver as would be required to arrive at the claimed compounds, and certainly no reason to do so. As such, the requirements for a *prima facie* case of obviousness have not been met. Thus, the §103 rejection is improper and should be withdrawn.

CONCLUSION

Applicants believe that the application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

Respectfully submitted,

Date October 15, 2008

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